TOBACCO INDUSTRY RESEARCH COMMITTEE

CONFIDENTIAL

TIRC Grant #72 — Progress Report #2

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Study the effect of methylcholanthrene on the tissues of the duck. To compare the effect of methylcholanthrene on different tissue with emphasis on reaction in the trachea when compared with the skin of the body and the web of the foot.

The money in this grant has been utilized in our experimental studies along with a grant from the United States Public Health Service.

The primary investigation has centered around a study of methylcholanthrene in the white Pekin duck. Emphasis has been on the type of tumor produced in the white Pekin duck in different anatomical sites. We have been interested in comparing the type of response in one portion of the body with that in another. A summary of these observations may be found in my most recent manuscript "Carcinogenesis in the Duck," of which you have a copy.

A new approach that we are now developing is to study the response in the trachea of the duck to methylcholanthrene. Our problem here has been to introduce methylcholanthrene into the trachea. Approximately 18 months ago we blew some crystals of methylcholanthrene into the trachea. These localized only in the proximal 3 or 4 cms. Our second attempt was to put 15 mgs. of methylcholanthrene per 1 cc. of mineral oil into the trachea. One-half cc. of this can be placed into the trachea daily for 15 to 20 days. Some of the ducks showed obstruction to the trachea and died. So far the percentage of deaths has been small. We have 25 of these birds under observation and we would like to continue observing them for a period of one year. I plan to increase this number to 50. Gross and histologic examinations are being followed on these tracheas.

During the past year we have been determining the presence or absence of methylcholanthrene in the skin and in the viscera following varying intervals of time after the carcinogen is last applied. Our results, like those of others, would show that methylcholanthrene disappears very rapidly after coming in contact with duck tissues. This study on the trachea is being followed in a similar manner. We are also using an ultra-violet light to demonstrate the presence or absence of methylcholanthrene in the tissues. These studies appear significant in helping us to evaluate the problem of carcinogenesis. In this connection it might be said that we have not observed any tumors in the liver; however, extensive degenerative changes have occurred. This would suggest that probably a break-down product of methylcholanthrene injures the liver and this break-down product is non-carcinogenic for the liver. Since the type of degeneration in the liver is similar to that produced by certain paraffin oils we now have some birds injected with paraffin oil to observe the hepatic lesions.

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One of the most interesting features of our entire study has been the spontaneous regression of the hemangiomas and the squamous cell carcinomas. Other investigators have produced metastasizing squamous cell tumors with methylcholanthrene in fowl. This apparently resulted from a much longer application of methylcholanthrene than we have used in our experiments. We now have a group of birds under observation in which we are continuing to apply methylcholanthrene in an attempt to obtain metastasizing squamous cell tumors. If this can be done, then we will have the problem of determining the mechanism by which these earlier lesions regress. There seems to be considerable clinical interest in the spontaneous regression of neoplasms in man. I feel that our studies may contribute to this overall problem. I am hoping that funds may be obtained which will enable me to grow these tumors on the chorio-allantoic membrane of the chick embryo and in the yolk sac. If we are able in this attempt, it will open up an exciting field with regard to these experimental lesions we are producing.

The following list of publications will indicate what we have been doing during the past year. Paper No. 5 should be out in the March number of Cancer Research. Paper No. 2 has been accepted by the Archives of Pathology. Paper No. 3 will be published as a part of the M. D. Anderson Symposium in Texas Reports on Biology and Medicine. Paper No. 1 has been submitted to Cancer. Paper No. 4 will be submitted to Cancer Research within the next few days.

1. Rigdon, R.H., Jack Walker, and A.H. Teddlie: Hemangiomas: An Experimental Study in the Duck. Submitted to Cancer, March 13, 1956.

2. Rigdon, R.H.: Trauma and Cancer. An Experimental Study in the Duck. Accepted by the Archives of Pathology.

3. Rigdon, R.H.: Carcinogenesis in the White Pekin Duck. Given at symposium at M. D. Anderson Hospital, Houston, March 28-31, 1956. To be published in Texas Reports on Biology and Medicine.

4. Rigdon, R.H.: Tumors Induced in Skin without Follicles. An Experimental Study in the Duck. Ready to be submitted.

5. Rigdon, R.H. and Murray D. Hooks: A Consideration of the Mechanism by which Squamous Cell Carcinomatoid Tumors in the Chicken Spontaneously Regress. Cancer Research, to be published March, 1956.

We appreciate your financial assistance to us in our experimental work. We hope that the work we have already done will justify you in continuing this aid. If there is any additional information, we will be happy to supply you with it.

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